reduced pressure to yield 50 mg of amorphous **11b**. High-resolution mass spectra were unobtainable. The infrared spectrum showed the loss of both the acetate carbonyl and the *N*-cyano bands: NMR ($CDCl_3$) δ 7.3 (1 H, s), 7.1 (1 H, s), 5.95 (2 H, s), 5.6 (1 H, s), 5.5 (1 H, s), 3.3 (3 H, s).

Hydrolysis of 11b. A sample (25 mg) of **11b** was dissolved in tetrahydrofuran/water (1:1) and a drop of 6 N hydrochloric acid was added. The solution was warmed on a steam bath and allowed to stand overnight. On evaporation at room temperature the product appeared as a crystalline solid, 10 mg, mp 205–210 °C dec, NMR [CH_3CN/D_2O (1/1)] δ 7.2 (1 H, s), 7.4 (1 H, s), 6.2 (2 H, s), 6.0 (1 H, s), 5.8 (1 H, s).

Reduction of 10 mg of the solid with 50 mg of lithium aluminum hydride in tetrahydrofuran for 1 h followed by a standard workup gave lycorine (**6b**, $R_3 = {}^1H$) identified by comparison of its mass spectrum and infrared spectrum with those of authentic lycorine.

Registry No.—**2a**, 477-20-3; **2b**, 477-19-0; **4a**, 517-99-7; **4b**, 548-11-8; **4c**, 476-29-9; **4d**, 517-78-2; **5**, 29477-83-6; **8**, 2492-05-9; **9**, 58958-43-3; **10**, 58944-33-5; **11a**, 58944-34-6; **11b**, 58944-35-7; **12**, 58958-42-2; *N*-ethyl hemipinimide, 27002-36-4; haemanthamine, 466-75-1; lycorine, 476-28-8; methylpseudolycorine α-epoxide, 58944-36-8; anhydromethylpseudolycorine, 58944-37-9; *o*-acetylpluviine, 58944-38-0; cyanogen bromide, 506-68-3.

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Crystal Structure and Absolute Configuration of Astrocasine Methobromide

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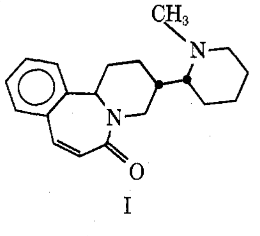
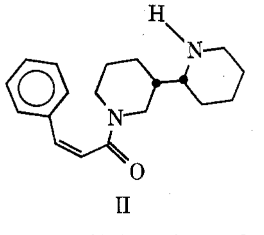
The determination of the crystal structure of the methanol-solvated methobromide of astrocasine, $(C_{21}H_{29}N_2O)^+Br^-\cdot CH_3OH$, confirms the molecular structure proposed by one of us and the absolute configuration was found to be the same as that of the biogenetically related alkaloid, astrophylline. Crystal data: orthorhombic, $P2_12_12_1$, $a = 7.654$ (1), $b = 8.678$ (1), $c = 32.589$ (3) Å, $Z = 4$, $d_x = 1.342$ g/cm^3, $d_m = 1.34$ (1) g/cm^3, x-ray intensity data were collected with an automatic diffractometer out to $\sin \theta/\lambda = 0.624$ Å^{-1} (3451 observed and 552 "unobserved" reflections.) The structure was solved using the heavy atom and "phase correction" methods. A final R factor of 3.1% (based on observed reflections) resulted.

Several new alkaloids[2–4] were isolated a few years ago from *Astrocasia phyllanthoides Robinson and Millspaugh,* a shrub belonging to the Euphorbiaceae family and growing in Central America.

A structure (I) was advanced[2] for the predominant alkaloid, astrocasine ($C_{20}H_{26}N_2O$, mp 171–172 °C) based mostly on spectral data (ir, uv, NMR, MS) and on a partial degradation. Later[3] the isolation of astrophylline ($C_{19}H_{26}N_2O$) from the same plant and its characterization as *N*-*cis*-cinnamoyl-3(*S*)-[2′(*R*)-piperidyl]piperidine (II) provided strong support for structure I. Astrophylline was the first *cis*-cinnamoyl alkaloid reported in nature and astrocasine is simply its cyclic analogue.



I



II

More recently[4] *N*-methylastrophylline, $C_{20}H_{28}N_2O$, and astrocasidine, $C_{20}H_{24}N_2O$, related to astrocasine but possessing an additional double bond conjugated with the aromatic ring, were also found in *A. phyllanthoides*.

Two alkaloids related to astrophylline, orensine and isoorensine, had been identified earlier in several *Adenocarpus* species (Leguminosae) by Ribas et al.[5] and both had been assigned *N*-*trans*-cinnamoyl tetrahydroanabasine skeletons; however, a later revision[6] indicated that isoorensine was the *cis*-cinnamoyl isomer of orensine.

A possible biogenetic pathway for demethylastrocasine and isoorensine,[4] postulating tautomerism of a charged intermediate, has been proposed as a variant of the scheme of Schütte et al.[7] for orensine.

Since the proposed structure for astrocasine contained a new and unique heterocyclic ring system, it seemed worth-

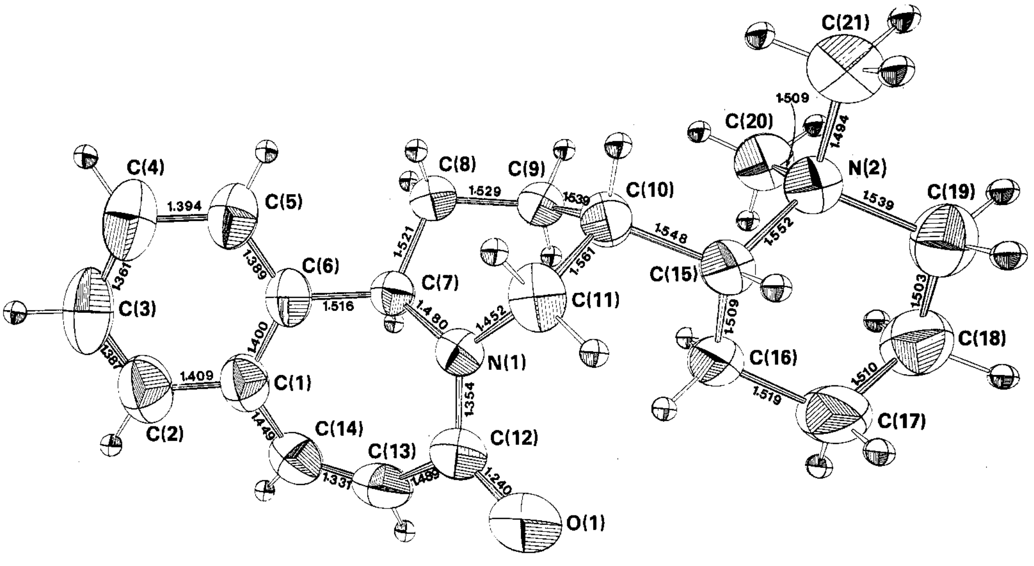


Figure 1. Crystal conformation and bond lengths of the astrocasine ion (thermal ellipsoids correspond to 50% probability). All bond lengths shown have esd's in the range of 0.003 to 0.006 Å. Hydrogen atom sizes are arbitrary.

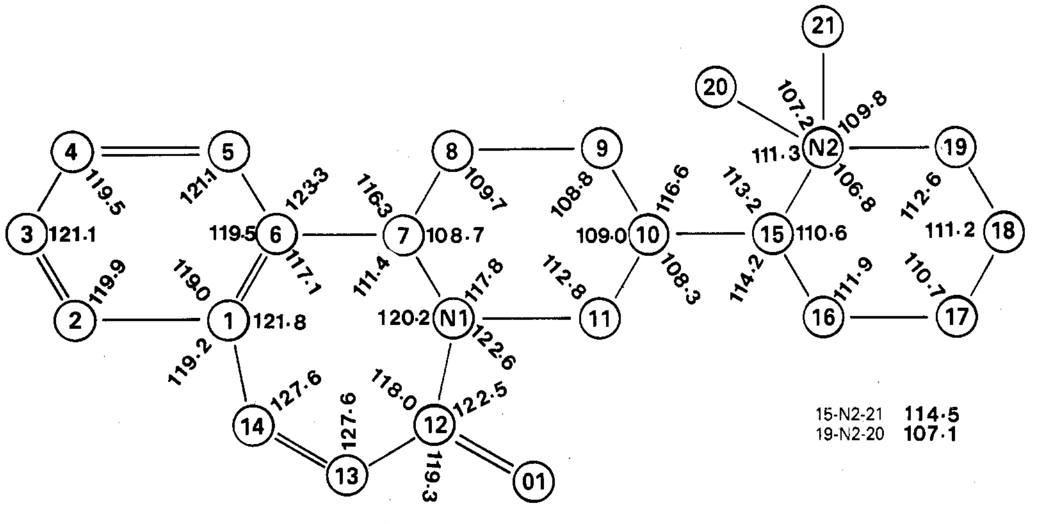


Figure 2. Bond angles in the cation. All angles have esd's ≤0.3°.

while to carry out an x-ray study and learn more about the structure, the conformational preferences, and the absolute configuration of this compound.

Discussion

A. Packing of Ions in the Crystal. The astrocasine cation has the three fused rings in a roughly planar conformation with the attached piperidine ring approximately parallel to the rest of the molecule. Most interionic contacts exceed van der Waals distances with only two values being less than 3.5 Å: C(8)–C(13), related by *a*, has a length of 3.47 Å and C(4)–C(11), related by the screw axis parallel to *b*, has a length of 3.43 Å. The packing is shown in Figure 4.

The packing of the cations is somewhat different from that which could be expected for un-ionized molecules in that they lie roughly on planes parallel to (010) and are not inclined to screw axes. Electrostatic forces between anions and cations presumably control the packing to a large extent since each bromide ion lies between two quaternary nitrogen atoms (related by the *b* translation) at distances of 4.239 and 4.880 Å and is also at a distance of 4.405 Å from another ionized nitrogen atom (related by the *a* screw axis to the first). The solvent molecules occupy spaces between the ions and appear to be held by O–H · · · Br hydrogen bonds of length 3.269 Å.

The thermal parameters of the solvent molecule indicate that the oxygen atom, despite being hydrogen bonded, is vibrating more than the carbon atom. However, the carbon atom is fairly close to several hydrogen atoms in astrocasine ions and may be held by van der Waals forces. The experiment of reversing the atomic types was tried and led to unrealistic thermal parameters. It is also not impossible that there is some positional disorder since the ease of loss of solvent molecules from the crystal indicates that the forces holding them are weak. The other thermal parameters appear consistent with the packing; the least vibrating parts of the astrocasine ion are those near the ionized nitrogen atom which is presumably held by the ionic forces. The phenyl ring has the largest thermal parameters and it can be seen from Figures 1 and 4 that its maximum vibration is in the ring plane which is in the direction where van der Waals forces are weakest.

B. Molecular Structure and Conformation. The piperidine ring containing the ionized nitrogen atom adopts a reasonably good chair conformation as may be seen from the torsion angles (Figure 3). The ring angle at N(2) is smaller than the tetrahedral angle but the average angle at the other atoms is 111.4° and the average torsion angle is 57.2° which may be compared with the corresponding angles of 111.1 and 55.8° given as best values for cyclohexane by Bucourt and Hainaut.[8] The C–N bond lengths show the expected expan-

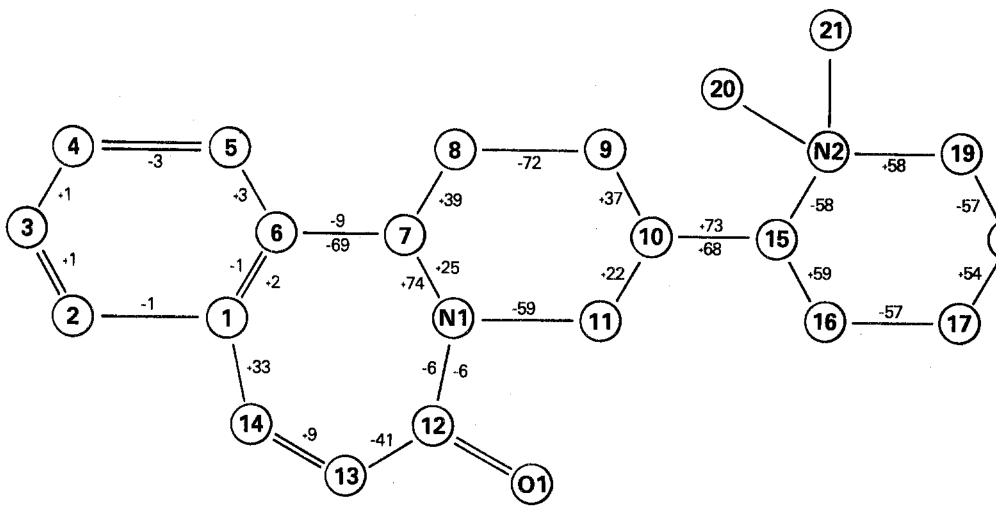


Figure 3. Torsion angles.[22]

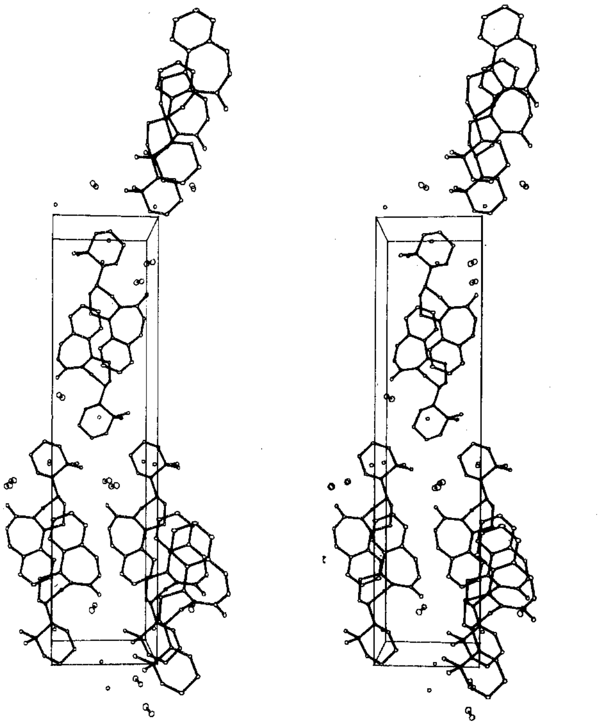


Figure 4. Packing diagram. The direction of projection is down *a*.

sion[9] from the standard un-ionized length[10] of 1.47 Å. The C–C bonds of the piperidine ring do not differ significantly in length (average 1.510 Å) but are all slightly shorter than the usual alkane C–C length of 1.54 Å.

In the rest of the cation, bond lengths are, within the esd's, essentially normal[10] except for the rather long C(10)–C(11) bond [1.561 (4) Å]. The long bond may result from strain introduced by the planar conformation at N(1). The single bond C(13)–C(12) has a length of 1.489 (5) Å, probably indicating some conjugation between the carbonyl carbon C(12) and the doubly bonded C(13) despite the torsion angle of −41°. The bond C(1)–C(14) has a length of 1.449 (5) Å and the conjugation may be greater corresponding to the smaller torsion angle (33°) of the bond. In the amide, the N(1)–C(12) bond is a little longer than the standard value of 1.322 Å but some strain may be present since N(1) is a bridgehead atom in a seven-member ring system.

The seven-membered ring adopts the boat conformation as may readily be seen by comparing the pattern of signs of torsion angles with those given by Bucourt.[11] The conformation is different from the corresponding cycloheptane conformation because of the restriction of rotation about the bonds C(1)–C(6), C(13)–C(14), and N(1)–C(12) and the ring, unlike that of cycloheptane, is essentially rigid. Since the rigidity of the C(1)–C(6) bond forces C(1) and C(6) to be on the same side of the plane of atoms C(7), C(14), and C(13) the adoption of the boat conformation is necessary.

Given the conformation of the seven-membered ring, the torsion angles on either side of the bond N(1)–C(7) have the same sign and thus the fused piperidine ring must adopt a "flexible", i.e., boat or twist-boat, conformation.[12] The pattern of torsion angles indicates the twist-boat conformation. There are two possible twist-boat conformations, but, with the one opposite to that observed, the hydrogen atoms on C(5) and C(19) would be too close to each other.

Experimental Section

The methobromide derivative of astrocasine (mp 261–262 °C) was prepared by passing a methanolic solution of astrocasine methiodide[2] through an anion exchange resin column (Amberlite IRA-401) which had been previously treated with potassium bromide. The resulting bromide was recrystallized with some difficulty from methanol. The crystals slowly decompose on exposure to the atmosphere, presumably owing to loss of solvent of crystallization, but are relatively stable sealed in the thin glass capillaries used in this investigation. The unit cell parameters were determined by least-squares refinement using 14 Bragg angles measured at $\pm\theta$ with an Enraf-Nonius CAD4 diffractometer. Crystal data: empirical formula, $C_{21}H_{29}N_2O\ Br{\cdot}CH_3OH$; asymmetric unit weight, 437.43 Daltons; crystal habit, orthorhombic prismatic (elongation *a*); space group $P2_12_12_1$ (No. 19); x-radiation, Cu Kα (λ = 1.5418 Å, graphite monochromator); a = 7.654 (1) Å, b = 8.678 (1) Å, c = 32.589 (3) Å; Z = 4; d_x = 1.342 g cm^{-3}; d_m = 1.34 g cm^{-3} (flotation in CCl_4/hexane); crystal size, cube of side 0.4 mm; linear absorption coefficient, 30.0 cm^{-1}; reflections, 4003 (on a basis of counting statistics, 552 reflections had intensities less than $3\sigma(I)$ and were regarded as unobserved); limiting sin θ/λ, 0.624 Å^{-1}. Data collection techniques were as in ref 13.

The data for astrocasine methobromide were collected first with Mo Kα x-radiation by the stationary-crystal stationary-counter method using a Picker diffractometer. The structure was solved by the heavy atom and "phase correction"[14] methods. Direct phasing by means of the bromine contribution did not give a recognizable picture since the bromine coordinates are very close to ($\frac{1}{2}$,$\frac{1}{2}$,$\frac{1}{2}$) and thus electron density maps phased by the bromine alone have almost exact mmm symmetry. Refinement by block diagonal least-squares methods resulted in an *R* factor of 9.8%. The results were judged unsatisfactory because of high standard deviations in bond lengths and angles, probably caused by decomposition of the crystal and resolution problems attributable to the long *c* axis of the crystal.

The data were then recollected on an Enraf-Nonius CAD-4 diffractometer using Cu Kα radiation. Because a determination of the absolute configuration was desired, both *hkl* and $\bar{h}kl$ were measured

Table I. Atomic Parameters for the Heavier Atoms ($\times 10^4$)[a]

Atom	x/a	y/b	z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Br (1)	5284 (1)	−5032 (1)	−4459 (1)	68 (1)	58 (1)	61 (1)	−7 (1)	1 (1)	−3 (1)
C (1)	2252 (4)	−6480 (3)	−2705 (1)	71 (2)	64 (2)	54 (2)	9 (2)	−16 (1)	−13 (1)
C (2)	1923 (5)	−6291 (4)	−3127 (1)	100 (3)	84 (2)	60 (2)	24 (2)	−27 (2)	−19 (2)
C (3)	3210 (6)	−5692 (3)	−3381 (1)	133 (3)	66 (2)	47 (2)	18 (2)	−13 (2)	−10 (1)
C (4)	4820 (5)	−5329 (3)	−3232 (1)	128 (3)	50 (2)	54 (2)	−1 (2)	13 (2)	−4 (1)
C (5)	5170 (4)	−5535 (3)	−2816 (1)	94 (2)	52 (1)	49 (1)	−9 (1)	10 (2)	−5 (1)
C (6)	3901 (4)	−6091 (3)	−2551 (1)	65 (2)	48 (1)	47 (1)	1 (1)	−6 (1)	−7 (1)
C (7)	4239 (3)	−6421 (2)	−2101 (1)	39 (1)	49 (1)	44 (1)	−1 (1)	1 (1)	−4 (1)
C (8)	6136 (3)	−6363 (3)	−1963 (1)	42 (1)	70 (2)	48 (1)	−3 (1)	1 (1)	−8 (1)
C (9)	6220 (3)	−6308 (3)	−1494 (1)	39 (1)	64 (2)	48 (1)	3 (1)	−2 (1)	−8 (1)
C (10)	5627 (3)	−4702 (2)	−1351 (1)	48 (1)	47 (1)	42 (1)	−9 (1)	−4 (1)	−2 (1)
C (11)	4107 (4)	−4138 (2)	−1633 (1)	69 (2)	42 (1)	47 (1)	2 (1)	−9 (1)	2 (1)
C (12)	1454 (3)	−5628 (3)	−1791 (1)	43 (1)	75 (2)	62 (2)	15 (1)	−6 (1)	−7 (1)
C (13)	619 (3)	−6835 (4)	−2050 (1)	41 (2)	93 (2)	81 (2)	−2 (2)	−8 (1)	−11 (2)
C (14)	900 (4)	−7122 (4)	−2445 (1)	55 (2)	90 (2)	74 (2)	−3 (2)	−20 (2)	−20 (2)
C (15)	5025 (3)	−4561 (2)	−899 (1)	46 (1)	42 (1)	43 (1)	1 (1)	−8 (1)	−1 (1)
C (16)	3570 (3)	−5650 (3)	−783 (1)	50 (2)	58 (2)	46 (1)	−2 (1)	1 (1)	1 (1)
C (17)	2838 (4)	−5291 (4)	−360 (1)	63 (2)	90 (3)	56 (2)	1 (2)	10 (1)	5 (2)
C (18)	4272 (4)	−5294 (4)	−42 (1)	79 (2)	95 (3)	42 (1)	6 (2)	4 (1)	2 (2)
C (19)	5736 (4)	−4232 (3)	−162 (1)	76 (2)	66 (2)	40 (1)	15 (2)	−10 (1)	−9 (1)
C (20)	7924 (4)	−3460 (3)	−672 (1)	60 (2)	57 (2)	69 (2)	−12 (1)	−17 (1)	−7 (1)
C (21)	7417 (4)	−6175 (3)	−557 (1)	61 (2)	53 (2)	64 (2)	15 (1)	−14 (2)	−4 (1)
C (S)	9377 (7)	−4003 (6)	−3943 (2)	128 (5)	117 (4)	146 (4)	−18 (4)	−36 (4)	−6 (3)
O (S)	9012 (5)	−5650 (5)	−3998 (1)	132 (3)	179 (4)	188 (4)	20 (3)	−45 (3)	50 (3)
O (1)	543 (2)	−4852 (3)	−1554 (1)	53 (1)	116 (2)	84 (1)	31 (2)	−4 (1)	−29 (1)
N (1)	3194 (2)	−5398 (2)	−1833 (1)	45 (1)	52 (1)	43 (1)	5 (1)	−3 (1)	−7 (1)
N (2)	6532 (2)	−4644 (2)	−582 (1)	49 (1)	44 (1)	45 (1)	3 (1)	−8 (1)	−3 (1)

[a] Esd's are given parenthetically and refer to the last figure quoted. The temperature factor used had the form $\exp - 2\pi^2 \cdot (\Sigma_i \Sigma_j U_{ij} a_i^* a_j^* h_i h_j)$.

Table II. Hydrogen Atom Parameters[a]

Atom	x/a	y/b	z/c	B
1	−989	−786	−257	8.1
2	−920	−651	−325	8.5
3	−698	−551	−366	8.6
4	−420	−488	−341	8.2
5	−363	−532	−270	7.0
6	−619	−747	−205	5.4
7	−327	−734	−205	6.1
8	−327	−549	−208	6.1
9	−457	−706	−137	6.2
10	−260	−648	−139	6.2
11	−339	−398	−139	5.8
12	−673	−351	−146	6.2
13	−542	−340	−183	6.2
14	−28	−747	−191	7.5
15	−548	−348	−87	5.6
16	−736	−562	−98	6.0
17	−594	−670	−77	6.0
18	−804	−603	−28	7.2
19	−768	−426	−36	7.2
20	−621	−499	+22	7.7
21	−527	−635	−1	7.7
22	−471	−318	−16	6.8
23	−337	−427	+5	6.8
24	−257	−243	−68	6.5
25	−116	−348	−46	6.5
26	−153	−368	−94	6.5
27	−200	−640	−81	6.7
28	−174	−617	−33	6.7
29	−345	−697	−50	6.7

[a] Positional coordinates are multiplied by 10^3.

and also used in the refinement. Crystals were mounted approximately along the *a* axis but, in order to minimize double reflection, were misaligned by about 5° on each goniometer arc. The orientation matrix was determined by the diffractometer. Three standard reflections were measured periodically and, since a significant linear decrease in intensity was observed during data collection, three scaling groups were used. Within each group, the drop in intensities of the standard reflections was about 3%.

Scattering factors for carbon, nitrogen, and oxygen[15] and the bromide ion[16] were taken from the "International Tables for X-Ray Crystallography" and, for bonded hydrogen, from Stewart, Davidson, and Simpson,[17] and calculations were carried out using the XRAY72 system.[18]

Using the previously obtained atomic positional and thermal parameters, the structure was refined for several cycles using a Peterson and Levy[19] type weighting scheme by block diagonal least-squares methods. The function minimized was $\Sigma w \Delta^2$. A difference synthesis showed significant peaks for all hydrogen atoms except for one methyl hydrogen atom, those bonded to the aromatic ring, and those of the solvent molecule. The relatively large thermal parameters of the atoms concerned may explain the difficulty experienced in locating their attached hydrogen atoms but the positions of the missing atoms were calculated where possible. Subsequent refinement to convergence was carried out using a full matrix least-squares approach, and a final *R* factor of 3.1%[20] resulted (based on observed reflections). Hydrogen atom parameters were not refined but were set at chemically reasonable values consistent with the difference map. Atomic parameters are given in Tables I and II, bond lengths in Figure 1,[21] bond angles in Figure 2, and torsion angles[22] in Figure 3. (The C–O bond length in the solvent molecule is 1.467 (7) Å.)

The absolute configuration was determined by selecting the 23 Friedel pairs of reflections which had the highest significant differences in the observed structure factors and comparing those values with the calculated dispersion-corrected structure factors. Twenty-two of the pairs were consistent with the configuration indicated in I and Figure 1. The anomalous dispersion correction for bromine, with Cu Kα x-radiation, is only ca. 1.5e and thus the observed differences in Friedel pairs are relatively small and absorption errors can account for the single discrepancy. It might also be noted that, at an *R* factor of ca. 6.5%, the ratio of the *R* factors for the two configurations also indicated that configuration I was correct.

Registry No.—Astrocasine methobromide, 55343-75-4.

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(1) The work described in the paper was submitted in partial fulfillment of the requirements for the Ph.D. degree (Georgetown University, 1974).

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Structures of Norditerpene Lactones from *Podocarpus* Species

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The crystal structure of sellowin B bromohydrin acetate ($C_{20}H_{21}O_7Br$) has been determined. The space group is $P2_1$ with cell dimensions $a = 10.060$ (5), $b = 6.127$ (4), $c = 16.037$ (6) Å, $\beta = 96.02$ (2)°, and $Z = 2$. The structure, solved using MULTAN and refined to $R = 0.053$, indicates sellowin B and related compounds to be 2,3-β rather than 1,2-α epoxides. Earlier chemical results are interpreted in light of the new structure.

In recent years, many norditerpene dilactones showing important biological activities have been isolated from *Podocarpus* species, ancient gymnosperms growing in scattered parts of the southern hemisphere.[3] These compounds are usually highly polar and hydrophilic, heavily oxygenated, and chemically refractory, in spite of the presence of the lactones and (usually) epoxide groups. The small number of interpreted reactions reported[4–7] includes almost exclusively simple functional group derivatization (alcohol to acetate or ketone) and unexpected transformations of the molecules.

Perhaps due to this refractory response to usual chemical reagents, and to unusual spectral characteristics of the compounds as well, recent x-ray analyses have revised the majority of the published structures[3] in the group. Thus, inumakilactone A, long supposed to possess a 1,2-α epoxide in ring A,[6] was shown by x-ray analysis to be in fact a 1,2-β epoxide (**1**).[8] This structural modification affected, by extension, the accepted constitutions of at least ten other compounds isolated from eight *Podocarpus* species in three continents and New Zealand, including the most widely distributed member of the group, nagilactone C (**2**).[3,7,8] By x-ray analysis of its p-bromobenzoate, podolactone A was shown to possess a 2,3-β epoxide (**3**)[9] rather than the 1,2-α group widely accepted.[3,10] By extension, at least five additional lactones from three *Podocarpus* species are subject to a similar modification. The present paper confirms that the structure of one of these five, from the Brazilian *P. sellowii,* likewise must be modified from a 1,2-α epoxide to a 2,3-β epoxide. Thus, no ring A epoxide in the series remains with its originally proposed structure, and interpretations of the chemistry of this group in these compounds[4,5] must be revised. Even a ring A alcohol, nagilactone A, was definitively assigned stereochemistry (**4**) only after an x-ray analysis.[11] It is also possible that a ring A olefin, podolactone D, could possess a 2,3 rather than a 1,2 double bond; unfortunately, this olefin does not react with peracid to form an epoxide,[12] and the reverse deepoxidation in nagilactone C (**2**) gave complete saturation of the ring,[4] though in the absence of a neighboring hydroxyl group olefin formation might be favored. The presence of a 2,3 double bond in podolactone D is rendered more probable by the x-ray study[13] which shows the closely related podolide (**5**) to contain this structural feature.

Reaction of sellowin B (published structure **6**)[3,4,14] with N-bromoacetamide under forcing conditions, in an attempt to functionalize the double bond and thereby give entry to a three-carbon side chain, gave exclusively a hygroscopic ring A bromohydrin, mp 204–208 °C, which was directly acetylated to a beautifully crystalline bromohydrin acetate. This compound was selected for x-ray analysis over the less satisfactorily crystalline tribromide (olefin dibromide + epoxide bromohydrin) produced by direct bromination of sellowin B.

X-ray analysis of the bromohydrin acetate revealed it to possess structure **7,** with the conformation depicted in Figure 1. Figure 2 gives bond lengths and bond angles, Figure 3 packing in the unit cell, Table I atomic coordinates, and Table II torsion angles for the rings in the molecule. The torsion angles reveal that rings A, B, and C approximate chair, 1,2-diplanar (sofa), and 1,3-diplanar conformations.[15] The torsion angles involving the acetate group are C2–C3–O17–C17 (124.7°), C4–C3–O17–C17 (−108.4°), C3–O17–C17–C21 (−174.8°), and C3–O17–C17–O18 (4.0°).